AMENDMENTS TO THE SPECIFICATION

Please insert the following two paragraphs below the Title and before the first sentence:

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a divisional of U.S. Serial No. 09/839,996, filed April 20, 2001, which is a divisional of U.S. Serial No. 08/296,791, filed August 25, 1994, now U.S. Patent 6,245,337.

This invention was made with government support under grant numbers HD 29678 and A1 23945 awarded by the National Institutes of Health. The government has certain rights in the invention.

Please replace the paragraph beginning at page 8, line 4, with the following amended paragraph:
Figures 6A, 6B, and 6C depict the nucleotide sequence (SEQ ID NO:1) and predicted amino acid sequence (SEQ ID NO:2) of hap gene. Putative –10 and –35 sequences 5' to the *hap* coding sequence are underlined; a putative *rho*-independent terminator 3' to the *hap* stop codon is indicated with inverted arrows. The first 25 amino acids of the protein, which are boxed, represent the signal sequence.

Please replace the paragraph beginning at page 8, line 11, with the following amended paragraph:
Figures 7A, 7B, 7C, 7D, 7E, 7F, 7G, and 7H depict a sequence comparison of the *hap* product and the cloned *H. influenzae* IgA1 proteases. Amino acid homologies between the deduced *hap* gene product and the *iga* gene products from *H. influenzae* HK368 (SEQ ID NO:3), HK61 (SEQ ID NO:6), HK393 (SEQ ID NO:4), and HK793 (SEQ ID NO:5) are shown. Dashes indicate gaps introduced in the sequences in order to obtain maximal homology. A consensus sequence for the five proteins is shown on the lower line. The conserved serine-type protease catalytic domain is underlined, and the common active site serine is denoted by an asterisk. The conserved cysteines are also indicated by asterisks.

Please replace the paragraph beginning at page 11, line 8, with the following amended paragraph:
As used herein, a protein is a "HAP protein" if the overall homology of the protein sequence to the amino acid sequence shown in Figure 6 (SEQ ID NO:2) is preferably greater than about 40-50%, more preferably greater than about 60% and most preferably greater than 80%. In some

embodiments the homology will be as high as about 90 to 95 or 98%. This homology will be determined using standard techniques known in the art, such as the Best Fit sequence program described by Devereux *et al., Nucl. Acid Res. 12*:387-395 (1984). The alignment may include the introduction of gaps in the sequences to be aligned. In addition, for sequences which contain either more or fewer amino acids than the protein shown in Figure 6, it is understood that the percentage of homology will be determined based on the number of homologous amino acids in relation to the total number of amino acids. Thus, for example, homology of sequences shorter than that shown in Figure 6, as discussed below, will be determined using the number of amino acids in the shorter sequence.

Please replace the paragraph beginning at page 27, line 19, with the following amended paragraph:

The variants typically exhibit the same qualitative biological activity and will elicit the same immune response as the naturally-occurring analogue, although variants also are selected to modify the characteristics of the polypeptide as needed. Alternatively, the variant may be designed such that the biological activity of the HAP protein is altered. For example, the proteolytic activity of the larger 110 kD domain of the HAP protein may be altered, through the substitution of the amino acids of the active site. The putative catalytic domain of this protein is GDSGSPMF (SEQ ID NO:7), with the first serine corresponding to the active site serine characteristic of serine type proteases. The residues of the active site may be individually or simultaneously altered to decrease or eliminate proteolytic activity. This may be done to decrease the toxicity or side effects of the vaccine. Similarly, the cleavage site between the 45 kD domain and the 100 kD domain may be altered, for example to eliminate proteolytic processing to form the two domains. Putatively this site is at residue 960.

Please replace the paragraph beginning at page 39, line 3, with the following amended paragraph:

Comparison of the deduced amino acid sequence of Hap with other proteins. A protein sequence similarity search was performed with the predicted amino acid sequence using the BLAST network service of the National Center for Biotechnology Information (Altschul *et al.*, 1990, supra). This search revealed homology with the IgA1 proteases of *H. influenzae* and *Neisseria gonorrhoeae*. Alignment of the derived amino acid sequences for the hap gene product and the IgA1 proteases from four different *H. influenzae* strains revealed homology across the extent of the proteins (Figure

7), with several stretches showing 55-60% identity and 70-80% similarity. Similar levels of homology were noted between the hap product and the IgA1 protease from *N. Gonorrhoeae* strain MS11. This homology includes the region identified as the catalytic site of the IgA1 proteases, which is comprised of the sequence GDSGSPLF (SEQ ID NO:8), where 2 is the active site serine characteristic of serine proteases (Brenner, 1988, Nature (London). 334:528-530; Poulsen *et al.*, 1992, J. Bacteriol. 174:2913-2921). In the case of Hap, the corresponding sequence is GDSGSPMF (SEQ ID NO:7). The *hap* product also contains two cysteines corresponding to the cysteines proposed to be important in forming the catalytic domain of the IgA proteases (Pohlner *et al.*, 1987, supra). Overall there is 30-35% identity and 51-55% similarity between the *hap* gene product and the *H. influenzae* and *N. gonorrhoeae* IgA proteases.

Please replace the paragraph beginning at page 43, line 1, with the following amended paragraph:
Consistent with the possibility that the *hap* gene product follows a similar fate, we found that DB117(pN187) produced a secreted protein approximately 110-kD in size that was absent from DB117(pGJB103) (Figure 10). This protein was also produced by DB117(pJS106), but not by DB117(pJ5102) or DB117(pJS105). Furthermore, the two mutants with transposon insertions within the *hap* coding region were deficient in this protein. In order to determine the relationship between *hap* and the secreted protein, this protein was transferred to a PVDF membrane and N-terminal amino acid sequencing was performed. Excessive background on the first cycle precluded identification of the first amino acid residue of the free amino terminus. The sequence of the subsequent seven residues was found to be HTYFGID (SEQ ID NO:9), which corresponds to amino acids 27 through 33 of the *hap* product.

On page 49, immediately preceding the heading "CLAIMS" please insert the enclosed text entitled "SEQUENCE LISTING"